

EXTENDED TREATMENT OF ALBIOTIC FOR THE TREATMENT OF MASTITIS IN NZ DAIRY COWS

It is common practice in New Zealand and overseas to extend the treatment duration of antibiotic therapy beyond three treatments, in an endeavour to improve mastitis cure rates. This practice has been shown to improve cure rates with many antibiotics.^{1,2,3,4,5,6} The New Zealand Dairy Cattle Formulary V2.0 states “Extended therapy for Gram positive pathogens: this has been shown to increase cure rates compared to standard three treatment regime. Likely to be of most benefit in *Staphylococcus aureus* infections.” This formulary was published in 2018 by The Society of Dairy Cattle Veterinarians of the NZVA.

The Ministry for Primary Industries (MPI) NZCP1 milk supply regulations, and NZ dairy companys’ milk supply agreements stipulate written advice must be obtained from the prescribing veterinarian for the milk withholding time to be observed following treatment of cows with vet medicines. It is the vet’s responsibility to advise the appropriate withholding periods (WHP). The veterinarian must apply their knowledge to set the WHP, which may include further research if this is not stated on the product labels.

When authorising the use of antibiotics, Veterinarians have an obligation to consider likely and appropriate use patterns and provide farmers with sufficient information in the authorisation to cover possible residue risks when products are used, whether this be “on-label” or “off-label”. The study presented in this Technical Bulletin aims to provide information to support robust Veterinarian recommendations for withholding periods for Albiotic following extended treatment.

Pharmacokinetics

Pharmacokinetics can be described as the body’s effect on a drug (e.g. absorption, metabolism and excretion, including the speed and efficacy of these processes). The correct antibiotic dose, and how and when the antibiotic is administered are important determinates to efficacy. Albiotic combines both time dependent (lincomycin), and concentration dependent (neomycin) antibiotics, which have proven synergy against *Staph aureus*⁷.

Neomycin is not absorbed from the mammary gland into the bloodstream so there is no increased risk of neomycin residues in meat or offal when treatment duration is extended. Lincomycin has been shown to be absorbed into plasma, and reaches steady state after two treatments. This means, the steady state will be maintained following additional treatments at the same treatment intervals⁸.

Objective

To determine the residues of lincomycin and neomycin in milk following administration of Albiotic intramammary when administered to dairy cows under both twice-a-day (TAD) and once-a-day (OAD) milking conditions.

Study Design

This Study was conducted under Good Laboratory Practice (GLP) with animal ethics approval from Eurofins Agrosience Animal Ethics Committee (approval number (AGRIHEALTH/GLP/16/01).

A total of 44 cows were enrolled in the study, and were randomly assigned to one of two treatment groups. One group of 22 cows were milked twice-a-day, and administered Albiotic to each quarter at each milking for six milkings (total of three days). The remaining 22 cows were milked once-a-day and administered Albiotic to each quarter at each milking for six milkings (total of six days).

The currently registered withholding period following three treatments was observed (TAD 60 hours; OAD 96 hours). At the first milking following completion of these withholding periods composite milk samples were collected from each cow at that milking and the subsequent 3 milkings. The samples were identified with cow number, date, hours from last treatment and trial number.

The concentration of both lincomycin and neomycin was determined by a previously validated HPLC/MS/MS method. The level of each antibiotic in all milk samples was compared to the maximum residue level (MRL) permitted in milk according to the NZ Ministry of Primary Industries ‘Food Notice: Maximum Residue Levels for agricultural compounds’. The results presented for this study follow the method for regulatory residue studies to determine the milk WHP for ACVM product registration.

Results

All milk samples for all cows (both once-a-day and twice-a-day milking) returned results that were below the MRL for both lincomycin and neomycin, at the first milking after the current label withholding period (60 hours (5 milkings) for twice-a-day cows and 96 hours (4 milkings) for once-a-day cows).

Twice A Day Milking

The concentration of lincomycin in the milk samples analysed ranged between <LOD (limit of detection 3 µg/kg) to 120.1 µg/kg. The neomycin concentration ranged from <LOD (50 µg/kg) to 1,309 µg/kg. By 72 hrs (6 milkings) after the last treatment, all cows had lincomycin levels in the milk below the MRL for lincomycin (150 µg/kg), and all of the cows had neomycin levels in the milk below the MRL for neomycin (1,500 µg/kg). The results are shown in figures 1 and 2.

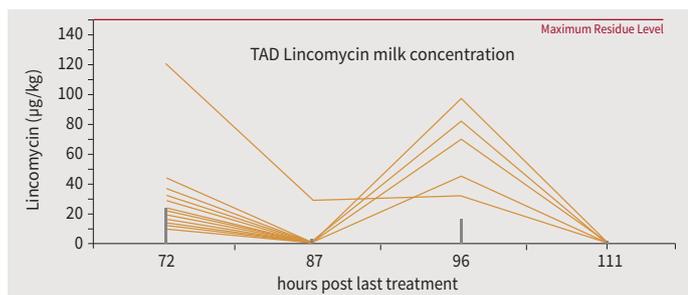


Fig 1. Summary of analytical results for lincomycin (µg/kg) in each individual cow at each milking for TAD cows, with mean for each time point shown as grey bar

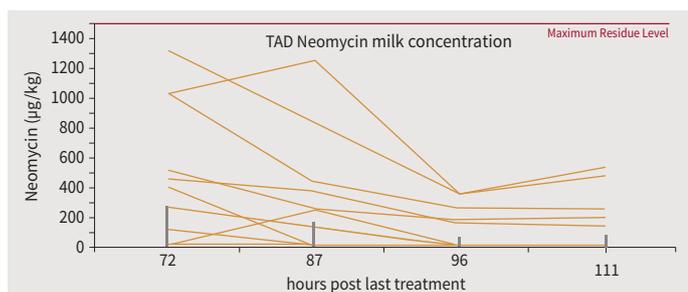


Fig 2. Summary of analytical results for neomycin (µg/kg) in each individual cow at each milking for TAD cows, with mean for each time point shown as grey bar

Once A Day Milking

The concentration of lincomycin in the milk samples analysed ranged between <LOD (3 µg/kg) to 28.93 µg/kg. The neomycin concentration ranged from <LOD (50 µg/kg) to 780.6 µg/kg. By 120 hrs (5 milkings) after the last treatment, all cows had lincomycin levels in the milk below the MRL for lincomycin (150 µg/kg), and all of the cows had neomycin levels in the milk below the MRL for neomycin (1500 µg/kg). The results are shown in figures 3 and 4.

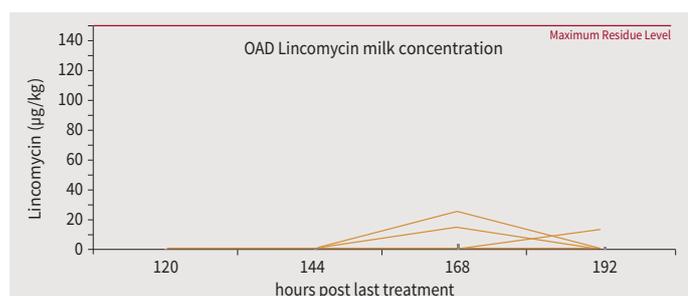


Fig 3. Summary of analytical results for lincomycin (µg/kg) in each individual cow at each milking for OAD cows, with mean for each time point shown as grey bar

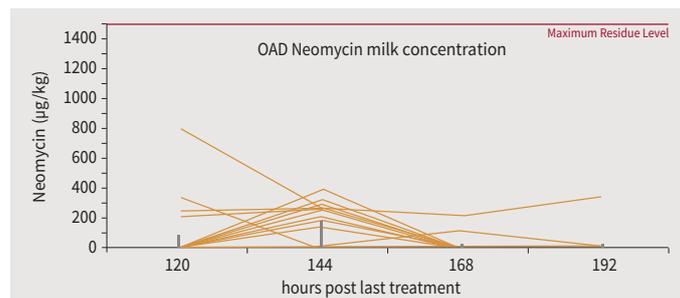


Fig 4. Summary of analytical results for neomycin (µg/kg) in each individual cow at each milking for OAD cows, with mean for each time point shown as grey bar

Conclusion

The current ACVM approved withholding period for Albiotic, when cows are treated at three consecutive milkings, is 5 milkings (60 hours) for cows being milked twice a day, and 4 milkings (96 hours) for cows milked once a day. This milk residue depletion study demonstrated that extending the course of treatment with Albiotic from three to six treatments resulted in antibiotic milk residues below the MRL for lincomycin and neomycin when these withholding periods were observed following completion of the treatment course.

This study meets the ACVM Research Standard and in summary shows that antibiotic milk residues from cows treated with Albiotic will not exceed MRL levels when cows are treated at either 3, 4, 5, or 6 consecutive milkings and comply with the above milk withholding period.

References

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- ⁸ Albiotic registration dossier. AgriHealth data on file.